Exhibit B: Peral et al., 1996, Am. J. Hum. Genet. 58:86-96.

In the Specification:

-- On page 30, please delete the second full paragraph and replace it with the following paragraph:

B1

The anti-polycystin-1 antibody was raised in rabbits against a purified synthetic 31 amino acid peptide corresponding to amino acids 4161-4191 in the predicted intracellular portion of polycystin-1, proximal to the C-terminal: sequence LPSRSSRGSKVSPDVPPPSAGSDASHPSTSS (SEQ ID NO: 1). Antiserum specificity was confirmed by Elisa, immunoblot and immunocytochemical analyses, before and after affinity purification; by lack of staining with pre-immune sera and competition of immunoreaction by preadsorption with the appropriate peptide. Immunocytochemistry was carried out using an avidin-biotin-peroxidase system (Vectastain, Vector Laboratories) and aminoethylcarbazole as chromogen 9 (red color). Staining patterns were identical when carried out on frozen and paraformaldehyde (4%)-fixed material. 1:500 dilution of anti-polycystin-1 was used.

In the Claims:

Please cancel Claims 1-20, and insert the following new Claims:

sub C1

21. A method for identifying a compound capable of modulating polycystin-1 activity, comprising:

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in an increase in cell adherence to type I collagen coated substrate;

(b) measuring cell adherence to type I collagen coated substrate; and

(c) comparing the level of cell adherence to type I collagen coated substrate obtained in (b) to the level of cell adherence to type I collagen coated substrate obtained in the presence of a vehicle control:

wherein if the level obtained in (b) differs from that obtained in the presence of a vehicle control, a compound capable of modulating polycystin-1 activity has been identified.

22. The method of Claim 21 wherein the cell is recombinantly engineered to express a mutant polycystin-1 protein.

23. The method of Claim 21 wherein the polycystin-1 protein is over expressed.

24. A method for identifying a compound capable of modulating polycystin-1 activity, comprising;

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in an increase in apical expression of NaK-ATPase on the cell membrane;

(b) measuring an increase in apical expression of NaK-ATPase on the cell membrane; and

(c) comparing the level of an increase in apical expression of NaK-ATPase on the cell membrane obtained in (b) to the level of an increase in apical expression of NaK-ATPase on the cell membrane obtained in the presence of a vehicle control:

wherein if the level obtained in (b) differs from that obtained in the presence of a vehicle control, a compound capable of modulating polycystin-1 activity has been identified.

25. The method of Claim 24 wherein the cell is recombinantly engineered to express a mutant polycystin-1 protein.

26. The method of Claim 24 wherein the polycystin-1 protein is over expressed.

Sub C3 27. A method for identifying a compound capable of modulating polycystin-1 activity, comprising;

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in an increased expression of ß-2-NaKATPase within the cell;

(b) measuring increased expression of ß-2-NaKATPase within the cell; and

(c) comparing the level of increased expression of ß-2-NaKATPase within the cell obtained in (b) to the level of increased expression of ß-2-NaKATPase within the cell obtained in the presence of a vehicle control:

wherein if the level obtained in (b) differs from that obtained in the presence of a vehicle control, a compound capable of modulating polycystin-1 activity has been identified.

28. The method of Claim 27 wherein the cell is recombinantly engineered to express a mutant polycystin-1 protein.

SUB C4 29. The method of Claim 27, 28 or 29 wherein the polycystin-1 protein is over expressed.

30. The method of Claim 7, 8 or 9 wherein the expression of ß-2-NaK-ATPase within the cell is measured using an anti-ß-2-NaK-ATPase antibody.

SUB C5 31. A method for identifying a compound capable of modulating polycystin-1 activity, comprising:

(a) contacting a test compound to a cell expressing a polycystin-1 protein wherein expression of said polycystin-1 protein results in a decreased incorporation of focal adhesion kinase into focal adhesion complexes;

(b) measuring a decreased incorporation of focal adhesion kinase into focal adhesion complexes; and

(c) comparing the level of a decreased incorporation of focal adhesion kinase into focal adhesion complexes obtained in (b) to the level of a decreased incorporation of focal adhesion kinase into focal adhesion complexes obtained in the presence of a vehicle control:

wherein if the level obtained in (b) differs from that obtained in the presence of a vehicle control, a compound capable of modulating polycystin-1 activity has been identified.

32. The method of Claim 31 wherein the cell is recombinantly engineered to express a mutant polycystin-1 protein.

SUB C6 33. The method of Claim 32 wherein the polycystin-1 protein is over expressed.

34. The method of Claim 31, 32, or 33 wherein the incorporation of focal adhesion kinase into focal adhesion complexes is measured using an anti-focal adhesion kinase antibody.

35. The method of Claim 31 wherein the cell expressing the polycystin-1 protein further comprises an epitope tagged focal adhesion kinase protein.

36. The method of Claim 22, 25, 28 or 32 wherein the recombinantly engineered cell comprises an epitope tagged polycystin-1 interacting protein.

37. The method of Claim 2, 3, 5, 6, 8, 9, 12 or 13 wherein the polycystin-1 protein is epitope tagged. --

REMARKS

Claims 1-10 are currently pending. Claims 1-10 are rejected under 35 U.S.C. § 112, first and second paragraph. Claims 1-10 have been canceled. New Claims 21-37 have been added to more particularly point out and distinctly claim the invention. No new matter is introduced by the amended claims and the claims are fully supported by the instant specification. For reasons set forth in detail below, Applicants request that the rejections be withdrawn and the claims be allowed to issued.

1. The Claims Are Enabled

Claims 1-10 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner alleges that while the specification is enabling for a method for identifying a compound capable of modulating polycystin-1 activity by measuring the expression of cell adherence to type I collagen coated substrate, apical expression of NaK-ATPase, or

expression of ß-2-NaK-ATPase, the specification does not reasonably provide enablement for a method for identifying a compound capable of modulating a variant of polycystin-1 activity by measuring any other mutant cell phenotype.

The test for enablement is whether one reasonably skilled in the art could make and use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. *U.S. v. Telectronics, Inc.* 857 F.2d 778 ??? 8 USPQ 2d 1217 (Fed. Cir. 1988) cert. denied, 490 U.S. 1046 (1989). Furthermore, a patent need not teach, and preferably omits, what is well-known in the art. *Lindermann, Maschinen fabrik GmBH* v. *American Hoist & Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984)..

Applicants assert that the instant specification, as filed, describes (i) methods for assaying cell adherence to type I collagen coated surfaces (p. 23, lines 4-17 of the specification); (ii) methods for assaying expression of NaK-ATPase or the ß2 subunit of NaK-ATPase on the cell membrane (p. 24, lines 3-14 of the specification); and (iii) methods for assaying incorporation of PKD proteins into focal adhesion clusters (p. 25, line 3 through p. 26, line 2 of the specification). In addition, with regard to claims encompassing the use of recombinantly engineered cells, the specification teaches how one would recombinantly engineer cells to express mutant forms of the PKD gene and/or overexpress the PKD gene and the expected mutant phenotype resulting from such expression.

Applicants assert that given the specific teachings of the specification, coupled with knowledge of the structure of the PKD-1 gene as well as mutant forms of the PKD gene, all of which are well established and well-known in the art (see Exhibit A and B),

one skilled in the art could readily carryout the screening methods of the invention without undue experimentation. The choice of mutant PKD genes and/or cells expressing the specified mutant phenotype is not critical so long as they function for purposes of the subject invention, as described above.

In view of the foregoing remarks and amendments to the claims, the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

2. The Claims as Amended are Definite

Claims 1-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner alleges that the phrase "such that" in Claim 1 renders the claim indefinite because it is unclear whether the limitation following the phrase is part of the claimed invention. To more particularly point out and distinctly claim the subject matter which applicant regards as the invention, Applicants have amended Claim 1 to replace "such that" with "wherein."

In view of the foregoing remarks and amendments to the claims, the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

CONCLUSION

Entry of the foregoing remarks into the file of the above-identified application is respectfully requested. The Applicant believes that the invention defined by the amended claims meets all the requirements for patentability. Withdrawal of all rejections and